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3. Travel medicine—prevention based on epidemiological data

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Abstract

In travel medicine efforts should be concentrated on preventive measures that are necessary, and travellers should be spared the side effects, costs and stress of superfluous measures. Excess mortality abroad is mainly due to traffic and swimming accidents, indicating the need for appropriate control strategies. The morbidity in travellers to developing countries is high, and is primarily due to traveller's diarrhoea. As prophylaxis is ineffective or unrealistic, and as travellers often need fast relief, it is recommended to include loperamide and an antimicrobial agent in the travel kit. Recent studies have shown that the incidence rate per month of *Plasmodium falciparum* malaria in Africa may reach 24/1000. The most frequently occurring immunizable diseases are hepatitis A (3/1000) and hepatitis B (0·8/1000). For many tourists and some expatriates pre-travel advice (hygiene, measures against mosquito bites, etc.) as well as chemoprophylaxis and immunization can be limited to these infections, but those travelling or staying outside large centres need additional measures.

Origin and present importance of travel medicine

Twenty years ago, the term travel medicine was unknown. However, even around 1600, young Rosalind asked the epidemiological question 'Alas, what danger will it be to us, maids as we are, to travel forth so far!' (*As You Like It,* act 1, scene 3, lines 104–105). The need to take preventive measures was also known, as exemplified by the warning 'Those girls of Italy, take heed of them' (*All's Well That Ends Well,* act 2, scene 1, line 19). For a long time medical advice for future travellers was based on anecdotal experience and not on firm data. It was probably KEAN (1963) who initiated modern travel medicine by assessing health risks in travellers and measures to reduce them.

The goal of travel medicine is to promote traveller's health, and this goes far beyond tropical medicine and parasitology, as aspects of other disciplines such as psychiatry, high altitude pathophysiology and behavioural sciences must also be considered. To develop rational guidelines for prevention of death and illness, it is necessary to balance the risks of dying and of morbidity against the risks, benefits and costs of prevention. The 20 million residents of industrialized nations who travel each year to developing countries (Fig. 1; IATA, 1990) especially need such guidelines, which should be known to practising physicians. I shall review the data on the risks of mortality and morbidity associated with travel and relate this information to available prevention measures.

Mortality data

In American travellers, the most frequent cause of death abroad was cardiovascular disease (Table 1),

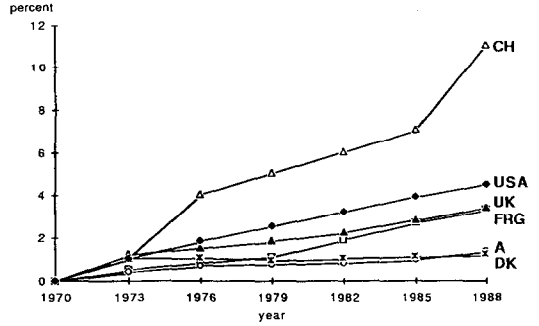

Fig. 1. Proportion of the population in industrialized nations which travels to developing countries per year.

Table 1. Fatalities among travellers abroad (percent)

Origin	US[a]		Swiss[b]		Swiss[b]	
Destination	Anywhere		Europe		Overseas	
Number	2463		247		68	
Year	1975/1984		1987		1987	
Cardiovascular	49		14		15	
Infection	1		–		3	
Other illness	?		2		9	
Road accident	7		13		12	
Air crash	2	25	4	23	12	44
Drowning	4		4		9	
Other injuries	12		2		11	
Unknown	25		58		29	

[a]From HARGARTEN *et al.* (1989).
[b]From LUSTENBERGER (1988).

but age-specific mortality rates were similar to those in the population remaining in the United States. Fatal infections were fairly successfully prevented; those which most often resulted in loss of lives were pneumonias. In contrast, death rates due to injury were increased by a factor of 2–3 in 15–44 year old travellers. Most fatal accidents were traffic or swimming accidents. Death statistics are incomplete, because no data are available on deaths which occur after return.

The following advice has been proposed to reduce fatal injuries: avoid using motorcycles and riding on the back of open trucks; avoid small, non-scheduled aircraft; avoid travel at night; use seat belts in cars, and require them as a condition of rental; use helmets, if bicycles or motorcycles cannot be avoided; carefully select swimming areas; and avoid alcohol and food before swimming (HARGARTEN *et al.*, 1989).

Car rental agencies should be required to provide seat belts. The cooperation of the travel industry would be helpful.

Morbidity data: general aspects

Up to 78% of short-term travellers to the tropics or to Europe reported some health impairment (KEN-

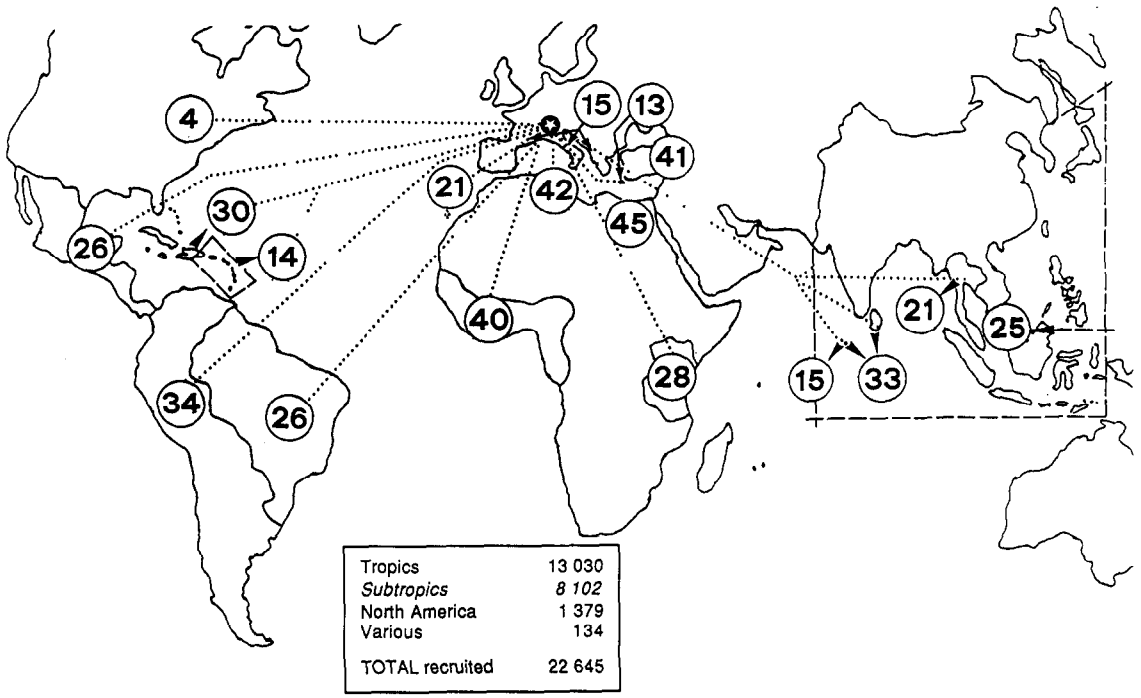

Fig. 2. Incidence of traveller's diarrhoea per 14 days of stay in 22 645 European tourists to various destinations.

DRICK, 1972; STEFFEN *et al.*, 1978; PELTOLA *et al.*, 1983; COSSAR & REID. 1989). The majority of these self-reported health problems were not severe: 21–43% felt ill, but only 5% needed medical attention, and <1% had to stay in a hospital, and then usually for only a few days. All studies showed that traveller's diarrhoea was the most frequent ailment of travellers to developing countries.

Traveller's diarrhoea (TD)

The incidence rates per two-weeks stay vary between destinations (Fig. 2) (STEFFEN *et al.*, 1983). Most of the data were assessed 8–10 years ago, but destinations in the southern and eastern Mediterranean were reassessed last in autumn 1989, and the rates remained virtually unchanged (BRENNER *et al.*, in press). There are 3 levels of risk for TD. Travellers originating in industrialized countries and staying for 2 weeks in Canada or the USA, northern and central Europe, Australia and New Zealand, show a low incidence rate, at most 8%. Intermediate incidence rates (8–20%) are found in most destinations of the Caribbean, in southern Europe, Israel, Japan and South Africa. In developing countries the incidence rates vary between 20 and 55%.

The incidence rates also vary depending on the origin of the travellers, with those living in northern Europe, the USA and Canada showing higher rates that those from southern Europe or developing countries (reviewed by STEFFEN & BOPPART, 1987). Infants and young adults show a particularly high incidence rate; in the former group TD is often severe (Pitzinger *et al.*, paper in preparation).

Most frequently, the symptoms of TD in tourists start on the third day of the stay abroad, with a second episode starting about a week after arrival in 20% of the cases. Untreated, the average duration of TD is 4 d, with 1% suffering over a month (STEFFEN & BOPPART, 1987). Usually traveller's diarrhoea takes a mild course, but concomitant symptoms may be very disturbing (Fig. 3); 22% of the patients show signs of mucosal invasive disease with fever and/or bloody stools.

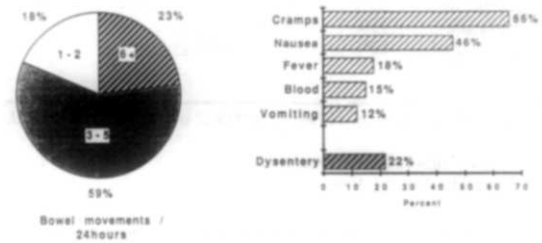

Fig. 3. Symptoms of traveller's diarrhoea.

There are various options for prevention of TD. Parents with infants who intend to travel just for pleasure to developing countries should postpone their journey. Immunization may be available in the future (LEVINE, 1990). Travellers must be informed that vaccines against typhoid or cholera will not prevent TD. Dietary restrictions such as the rule of 'boil it, cook it, peel it, or forget it' clearly reduce the incidence, but within the first 3 d of a stay in Kenya or Sri Lanka, 98% of Swiss tourists were eating salads, puddings, sandwiches with mixed fillings, using ice cubes in their drinks, or even choosing raw oysters or beefsteak tartare (KOTZICKI *et al.*, 1985). It is not known whether travellers from other nations are

more disciplined. Many drugs have been proposed for prophylaxis of TD (Table 2), but only antimicrobial agents are effective. They are not indicated for every traveller, but may be considered for stays of less than 2 weeks duration for travellers in whom dehydration and electrolyte imbalance might be particularly harmful to an underlying illness, for travellers with impaired immune defence, and possibly for 'very important persons' who have to eat what their hosts in the third world offer them.

Because of the unsatisfactory prophylactic means against TD, self-therapy abroad is important. In most cases, it would be reasonable just to wait until the symptoms of the self-limiting illness subside, meanwhile replacing fluid and electrolyte losses, but travellers want an immediate cure as, e.g., they may wish to go with their group to the next safari lodge. Oral rehydration therapy is the most important means of curing diarrhoeas in inhabitants in the third world and it is also indicated in small children and elderly patients with TD, but the oral rehydration salts actually marketed will in fact tend to increase the number of unformed bowel movements (WHO, 1988). Various studies have shown that loperamide is the fastest acting agent to treat non-invasive traveller's diarrhoea (Table 2), and there is no indication that complications may occur in such cases. This is the treatment of choice in mild to moderate, non-invasive illness, but it is contraindicated in dysentery (DUPONT & HORNICK, 1973; STEFFEN *et al.*, 1984). Combination therapy with loperamide plus trimethoprim/sulfamethoxazole results in faster disappearance of symptoms with a mean duration of illness of one hour, which is difficult to improve

Table 2. Efficacy and tolerance of agents used for prophylaxis and self-therapy of traveller's diarrhoea[a]

Drug	Efficacy		Side effects
Prophylaxis			
Lactobacilli	None		–
Difenoxin	Negative		Constipation
Bismuth s'sal.	40–70%		Few constipation, nausea
TMP/SMX[b]	80%		Allergy
Streptotriad	30–60%		Few allergies
Doxycycline	75%		Photosensitivity, diarrhoea
Mecillinam	75%		None recorded
Erythromycin	100%?		Allergy
Norfloxacin	88–93%		Not significant
Self-therapy	4 h	48 h	
Charcoal	None	None	–
Lactobacilli	None	None	–
ORS[c]	–	++	Initially more diarrhoea
Loperamide	41%	77%	More diarrhoea in dysentery
Bismuth s'sal	19%	76%	Black stools, black tongue
TMP/SMX[b]	22%	82%	Allergy
Doxycycline	12%	87%	Allergy, photosensitivity
Fleroxacine	15%	60%	Allergy
Loperamide+ TMP/SMX[b]	65%	85%	Allergy

[a]Sources: ERICSSON *et al.* (1990); STEFFEN *et al.* (1988); SCOTT *et al.* (1990).
[b]Trimethoprim+sulphamethoxazole.
[c]Oral rehydration solution.

Table 3. Malaria: morbidity and mortality without chemoprophylaxis[a]

Destination	Incidence rate per month per 10^6	Case fatality rate (%)	Mortality rate per month per 10^6
West Africa			
British	6810[b]	2	136
Other European	24000	2	480
East Africa			
British	1960[b]	2	40
Other European	15000	2	300

[a]Sources: PHILLIPS-HOWARD *et al.* (1990), STEFFEN *et al.* (1990).
[b]Attack rate per journey.

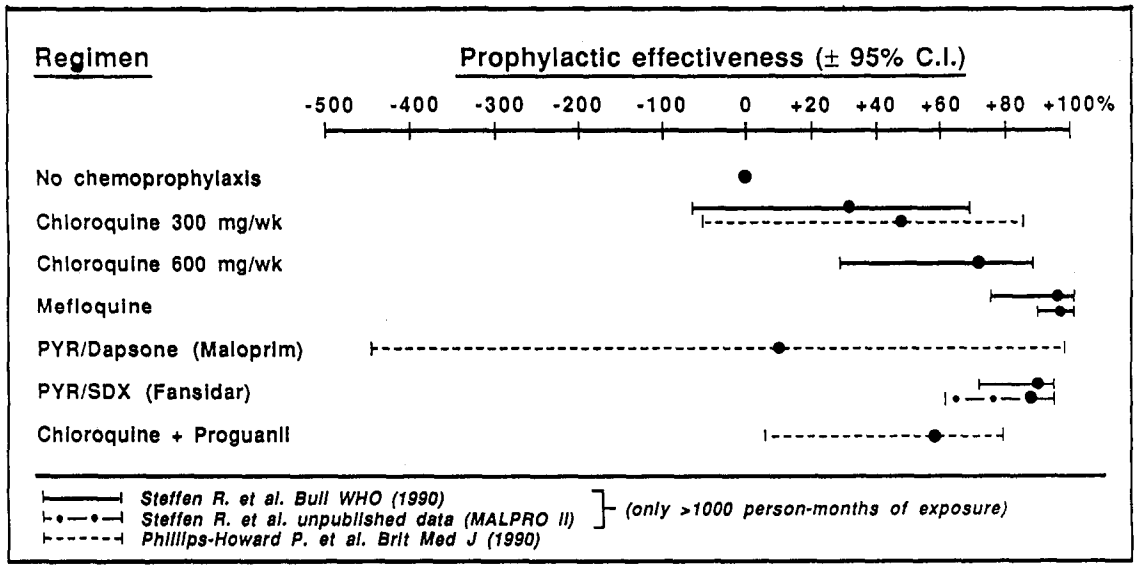

Fig. 4. Prophylactic effectiveness of various regimens of malaria chemoprophylaxis in East Africa.

(ERICSSON *et al.*, 1990). Those 2 drugs can be recommended for the travel kit. Ultimately, it should be possible to have a single drug for self-therapy, or—even better—to have hotels where travellers do not acquire TD.

Malaria

Two recent studies (PHILLIPS-HOWARD *et al.*, 1990; STEFFEN *et al.*, 1990) give an account of the morbidity of malaria in travellers who have visited Africa without using chemoprophylaxis (Table 3), and both illustrate the importance of this infection. If there is a difference between the 2 studies, it may be due to differences in design. The British study was based on reports to the Malaria Reference Laboratory and, therefore, cases diagnosed abroad were not included and notification of cases was incomplete; in addition, only attack rates were presented. In our own surveys, the second of which is still in progress, cohorts of travellers recruited aboard British, German and Swiss charter flights returning from East Africa are being followed up.

Analysis of the effectiveness of various chemoprophylactic regimens—unadjusted for compliance and probably a better reflection of real conditions than the efficacy in compliant users—shows that, in East Africa, chloroquine 300 mg base per week failed to protect travellers in the 3 studies summarized in Fig. 4. In contrast, mefloquine, and to a lesser extent chloroquine plus proguanil, offered fair or even good protection. Similar results were found in West Africa. Furthermore, an observational, uncontrolled study of Peace Corps volunteers showed that even higher effectiveness could be achieved with mefloquine, if given at weekly instead of bi-weekly intervals (LOBEL *et al.*, 1991).

Malaria chemoprophylaxis is associated with 20–25% of self-reported adverse effects, 60% of which are only slight. Similar rates of medical consultations for adverse events were reported with all drugs. As shown in Table 4, mefloquine had a similar pattern of adverse events as chloroquine, except that it was significantly more often associated with dizziness. In 17 000 prophylactic mefloquine users one patient (using continuous antiepileptic medication) was admitted to hospital for a seizure, which indicates the rarity of severe neuropsychiatric reactions (WHO, 1989).

Some experts recommend that travellers should carry standby reserve medication for self-therapy or for use by the local doctor. When standby medication was available, it was used by about 4% of travellers to Africa. Mefloquine in a dosage of 750–1500 mg/24 h was associated with nausea and dizziness in 30–50%. It is not known how often use of standby medication was justified.

Malaria diagnosis is often delayed. In each of the 4 cases who died of malaria in our first cohort of 44 000 travellers, diagnosis was late, some physicians believing that their patients could not develop severe malaria under chloroquine prophylaxis (LOBEL, 1985; STEFFEN *et al.*, 1990).

Sexually transmitted diseases (STDs)

Casual sexual contacts abroad may play a major role in the transmission of human immunodeficiency virus (HIV) (BLAXHULT & BÖTTIGER, 1989) and other STDs (DE SCRYVER & MEHEUS, 1989). In a pilot study investigating the frequency and characteristics of casual sexual contacts of Swiss short-term visitors to developing countries, casual sexual contacts were frequently reported (Table 5). The participants in many of these contacts were unprotected by condoms, partly due to drunkenness (STRICKER *et al.*, 1990). Intervention studies must determine how future travellers can best be influenced to protect themselves.

Table 5. Casual sexual contacts of Swiss tourists in tropical Africa, the Far East and Latin America, 1987/1988[a]

Group	High risk[b]	Comparison[c]
Casual sexual contacts	49/82 (67%)	5/166 (4%)
Type of contacts		
Prostitutes	27/55 (49%)	
Other indigenous	26/55 (47%)	
Only Europeans	2/55 (4%)	
>3 partners	14/55 (25%)	
Condom use		
Men, aged 20–39 years	27/34 (79%)	
Men, aged ≥40 years	4/15 (27%)	
Women[d]	0/6 (0%)	

[a]Source: STRICKER *et al.* (1990).
[b]Attenders at vaccination centres.
[c]Random sample of airline charter passengers.
[d]Use by partner.

Table 4. Adverse events reported by travellers and attributed to malaria chemoprophylaxis (percent)

	No chemoprophylaxis	Chloroquine 300 mg/ week	Chloroquine 600 mg/ week	Mefloquine	Proguanil	PYR/ SDX[a]	PYR/SDX[a] +Mefloquine	Chloroquine +Proguanil
Number of subjects	566	363	773	9243	82	4478	145	930
Nausea	0·7	8·0	9·6	11·2	9·8	7·1	6·9	15·2
Mouth ulcers	0	1·1	0·9	1·1	4·9	0·7	0·7	4·3
Headache	0·7	5·0	4·1	6·1	1·2	3·9	4·1	5·2
Dizziness	0·5	3·9	4·4	6·9	0	3·3	2·8	4·2
Visual problems	0·2	4·4	4·3	2·0	2·4	1·6	1·4	1·7
Depression	0	0·3	1·0	1·2	0	0·7	1·4	2·0
Insomnia	0	5·8	2·6	4·1	6·1	2·5	3·4	4·1
Any adverse event	1·4	24·2	23·9	22·7	20·7	16·9	17·2	28·1

[a]Pyrimethamine+sulfadoxine.

Immunizable diseases

Table 6 shows that immunizable infections are far less a threat to travellers than malaria, and that of these infections the various hepatitis serotypes are the most important.

Hepatitis

Various retrospective studies (STEFFEN *et al.*, 1977; SKINHØJ *et al.*, 1981; APOTHÉLOZ *et al.*, 1982; IWARSON & WAHL, 1983) and one follow-up study (STEFFEN *et al.*, 1987) have investigated the risk of imported hepatitis. The hepatitis attack rates did not differ significantly between regions, or even individual countries, within the developing world. Hepatitis A is the most frequent serotype of hepatitis imported from the third world; it is responsible for about 60% of hepatitis cases in returning travellers. Hepatitis B and hepatitis non-A, non-B (now C and E) were each diagnosed in about 15% of the cases, while some 10% remained unclassified. In contrast, hepatitis A played only a minor role in infections acquired within Europe. In the follow-up study, 8 of almost 8000 travellers to various developing countries, the majority having stayed in luxury hotels, were diagnosed as having symptomatic hepatitis A. Their mean duration of incapacity to work was 33 d. Only a French group has published a hepatitis A seroconversion study in unprotected volunteers working in the 'bush' of Central or West Africa, of whom 19/1000 seroconverted per month, the majority with jaundice (LAROUZÉ *et al.*, 1987).

The available retrospective, follow-up and seroconversion data suggest that the incidence rate of symptomatic hepatitis A for a one-month journey from an industrialized country to a developing country is about 3(–6)/1000 for the usual non-immune traveller. The risk seems to be 6 times as great in hikers or other persons who eat and drink under poor hygienic conditions.

As recently reviewed (STEFFEN, 1990), professional people working in developing countries are at high risk of hepatitis B. They have a monthly incidence of symptomatic or asymptomatic hepatitis B of 80–420/100 000, with 20–60/100 000 being symptomatic. In contrast, tourists have a very low incidence, unless they disregard basic hygienic rules.

Typhoid fever

Several surveys have documented the attack rate of imported typhoid fever (STEFFEN, 1982; TAYLOR *et al.*, 1983; PHLS, 1984). All showed rates of 1 in 30 000. In India, Senegal and North Africa a ten-fold higher risk was found (SCHOTTENHAML, 1989). Persons travelling off the beaten track were at higher risk. The case fatality rate did not exceed 1%.

Poliomyelitis

Recently, 47 cases of imported poliomyelitis in residents of Europe, Canada or the USA, who often had been in the third world for less than a week, were reviewed (KUBLI *et al.*, 1987). As asymptomatic infections are far more frequent than symptomatic ones, we must assume that the incidence of infection in unvaccinated travellers is at least 20 per 1 000 000. Surprisingly, only 18 contact cases in industrialized nations were recorded.

Table 6. Morbidity and mortality of immunizable diseases in 1 000 000 non-immune travellers visiting developing countries[a]

Infection	Incidence rate per month	Case fatality rate (%)	Mortality rate per month
Hepatitis A	3000 (–6000)	0·1	3 (–6)
Hepatitis B, expatriates (symptomatic or asymptomatic)	800 (–2400)	2	16 (–48)
Typhoid	30	1	0·3
India, N/NW Africa	300	1	3
Poliomyelitis			
Symptomatic	4	20	0·2
Asymptomatic	20 (–1000)	–	? in contacts
Cholera	3	2	0·06

[a]No data available for diphtheria, Japanese encephalitis, measles, meningococcal meningitis, rabies, tetanus, tuberculosis, yellow fever.

Cholera

Cholera is rarely imported into industrialized countries. Between 1975 and 1981 only 129 such cases were reported to the World Health Organization. Detailed analysis showed an attack rate of 2 in 1 000 000 (SNYDER & BLAKE, 1982; MORGER *et al.*, 1983). All infected patients had a short stay in hospital, and the case fatality rate in travellers was below 2%. Apparently, cases are rarely treated abroad and asymptomatic imported infections do not cause epidemics.

Yellow fever

Yellow fever is the only immunization which may be required by health authorities in the third world from travellers arriving from industrialized countries. Only 5 cases in travellers (4 unvaccinated) have been published in the last 10 years, due to the fact that immunization is required.

Rare immunizable diseases

No data exist on the risk of Japanese encephalitis and meningococcal disease, which have only rarely and anecdotally been described in civilian travellers; the latter usually occurred in situations in which travellers lived in crowded conditions. It is impossible to guess at an incidence rate; it is probably below 1 in 1 000 000. Just one plague case has been reported in an international traveller since 1966 (ANONYMOUS, 1991). In contrast, many cases of rabies in travellers have been reported, but again there are insufficient data to estimate rates of exposure (NICHOLSON, 1990). The incidence of animal bites in expatriates living in the third world is 2% (Brunner, personal communication). Imported measles is responsible for 26% of all cases in the USA. Surprisingly, there are hardly any published data on diphtheria or tetanus in travellers.

Conclusions concerning immunization

Being aware of epidemiological data, various strategies of immunization for travellers can be considered. One strategy is to immunize against every potential risk. Some travellers may thereafter have a 'St Sebastian syndrome', and feel like the Roman officer who was tortured with arrows which were not to kill him. The minimal option would be based on

cost versus benefit considerations, but not even immunoglobulin prophylaxis results in a ratio which clearly shows that it is necessary. Thus, every physician will have to decide at which morbidity and mortality rates he wants to draw the line, above which he does, and below which he does not, immunize. Above all, he should not protect his travellers against rare risks, while leaving them unprotected against more important ones. For reasons unrelated to travel, Europeans should be immune against poliomyelitis, tetanus and diptheria, as well as against measles, mumps and rubella. Travellers should be encouraged to receive immunoglobulin and, hopefully, soon active combined hepatitis A and B vaccine. As long as the prices for the latter stay above £30 per dose, it may well be reserved for those working abroad. The indication for typhoid vaccine can be restricted to those eating and drinking off the beaten track (USA, 1989; WHO, 1990). Immunization against rare infections is reserved for travellers who are likely to be at unusually high risk. We must realize that if future travellers expect too many injections, they may avoid their doctors and neglect to take important prophylactic measures.

References

Anonymous (1991). Imported bubonic plaque—District of Columbia. *Morbidity and Mortality Weekly Report*, **39**, 895–896.

Apothéloz, M., Grob, P. J., Steffen, R. & Schär, M. (1982). Welchen Auslandreisenden ist ein Impfschutz gegen Hepatitis zu empfehlen? *Sozial- und Präventivmedizin*, **28**, 264–265.

Blaxhult, A. & Böttiger, M. (1989). Varannan HIV-smittad heterosexuell svensk har blivit infecterad unter utlandsvistelse. *Läkartidningen*, **86**, 4215–4219.

Brenner, D., Steffen, R. & Schorr, D. (in press). Traveller's diarrhoea in Egypt, Tunisia and Turkey 1989. *Travel Medicine International*.

Cossar, J. H. & Reid, D. (1989). Health hazards of international travel. *World Health Statistics Quarterly*, **42**, 61–69.

De Schryver, A. & Meheus, A. (1989). International travel and sexually transmitted diseases. *World Health Statistics Quarterly*, **42**, 90–99.

DuPont, H. L. & Hornick, R. B. (1973). Adverse effect of Lomotil therapy in shigellosis. *Journal of the American Medical Association*, **226**, 1525–1528.

Ericsson, C. D., DuPont, H. L., Mathewson, J. J., Stewart West, M., Johnson, P. C. & Bitsura, J. A. M. (1990). Treatment of traveler's diarrhoea with sulfamethoxazole and trimethoprim and loperamide. *Journal of the American Medical Association*, **263**, 257–261.

Hargarten, S. W., Baker, T. & Guptil, K. (1989). Fatalities of American travelers—1975, 1984. In: *Proceedings: First Conference on Travel Medicine*, Steffen, R., Lobel, H. O., Haworth, J. & Bradley, D. J. (editors). London & New York: Springer, pp. 55–64.

IATA (1990). *International On-flight Statistics*. Geneva: International Air Transport Association.

Iwarson, S. & Wahl, M. (1983). Hepatitis A in Swedish foreign travellers. *Development of Biological Standardization*, **54**, 419–422.

Kean, B. H. (1963). The diarrhea of travelers to Mexico. *Annals of Internal Medicine*, **59**, 605–614.

Kendrick, M. A. (1972). Study of illness among Americans returning from international travel, July 11–August 24, 1971. *Journal of Infectious Diseases*, **126**, 684–687.

Kozicki, M., Steffen, R. & Schär, M. (1985). 'Boil it, cook it, peel it, or forget it': does this rule prevent travellers' diarrhoea? *International Journal of Epidemiology*, **14**, 169–172.

Kubli, D., Steffen, R. & Schär, M. (1987). Importation of poliomyelitis to industrialized nations between 1975 and 1984: evaluation and conclusions for vaccination recommendations. *British Medical Journal*, **195**, 169–171.

Larouzé, B., Gaudebout, C., Mercier, E., Lionsquy, G., Dazza, M. C., Elias, M., Gaxotte, P., Coulaud, J. P. & Ancelle, J. P. (1987). Infection with hepatitis A and B viruses in French volunteers working in tropical Africa. *American Journal of Epidemiology*, **126**, 31–37.

Levine, M. M. (1990). Modern vaccines—enteric infections. *Lancet*, **335**, 958–961.

Lobel, H. O. (1985). Fatal malaria in US civilians. *Lancet*, **i**, 873.

Lobel, H. O., Bernard, K. W. & Williams, S. L. (1991). Effectiveness and tolerance of long term malaria chemoprophylaxis with mefloquine: need for better dosing regimen. *Journal of the American Medical Association*, **265**, 361–368.

Lustenberger, I. (1988). *Todesfälle von Schweizern in Ausland*. Thesis, University of Zurich.

Morger, H., Steffen, R. & Schär, M. (1983). Epidemiology of cholera in travellers and conclusions for vaccination recommendations. *British Medical Journal*, **286**, 184–186.

Nicholson, K. G. (1990). Rabies. *Lancet*, **335**, 1201–1205.

Peltola, H., Kyrönseppä, H. & Hölsä, P. (1983). Trips to the south—a health hazard—morbidity of Finnish travellers. *Scandinavian Journal of Infectious Diseases*, **15**, 375–381.

Phillips-Howard, P. A., Radalowicz, A., Mitchell, J. & Bradley, D. J. (1990). Risk of malaria in British residents returning from malarious areas. *British Medical Journal*, **300**, 499–503.

PHLS (1984). Communicable Disease Report. *Community Medicine*, **6**, 72–75.

Schottenhaml, C. (1990). *Typhusepidemiologie in der Schweiz 1984 bis 1987 und Beurteilung der Wirksamkeit des Typhusimpfstoffes Vivotif*. Thesis, University of Zurich.

Scott, D. A., Haberberger, R. L., Thornton, S. A. & Hyams, K. C. (1990). Norfloxacin for the prophylaxis of travelers' diarrhea in US military personnel. *American Journal of Tropical Medicine and Hygiene*, **42**, 160–164.

Skinhøj, P., Gluud, C. & Ramsøe, K. (1981). Traveller's hepatitis. *Scandinavian Journal of Infectious Diseases*, **13**, 1–4.

Snyder, J. D. & Blake, P. A. (1982). Is cholera a problem for US travelers? *Journal of the American Medical Association*, **247**, 2268–2269.

Steffen, R. (1982). Typhoid vaccine, for whom? *Lancet*, **i**, 625–616.

Steffen, R. (1990). Risks of hepatitis B for travellers. *Vaccine*, **8**, 31–32.

Steffen, R., Regli, P. & Grob, P. (1977). Wie gross is das Risiko einer Reisehepatitis? *Schweizerische Medizinische Wochenschrift*, **107**, 1300–1307.

Steffen, R., van der Linde, F. & Mayer, H. E. (1978). Erkrankungsrisiken bei 10.500 Tropen- und 1300 Nordamerika-Touristen. *Schweizerische Medizinische Wochenschrift*, **108**, 1485–1495.

Steffen, R., van der Linde, F., Gyr, K. & Schär, M. (1983). Epidemiology of diarrhea in travelers. *Journal of the American Medical Association*, **249**, 1176–1180.

Steffen, R., Stransky, M. & Kozicki, M. (1984). Vorbeugende Massnahmen gegen Reisediarrhöe. *Schweizerische Medizinische Wochenschrift*, **114**, supplement 17, 38.

Steffen, R., Rickenbach, M., Wilhelm, U., Helminger, A. & Schär, M. (1987). Health problems after travel to developing countries. *Journal of Infectious Diseases*, **156**, 84–91.

Steffen, R., Heusser, R., Tschopp, A. & DuPont, H. L. (1988). Efficacy and side-effects of six agents in the treatment of travelers' diarrhoea. *Travel Medicine International*, **6**, 153–157.

Steffen, R., Heusser, R., Mächler, R., Bruppacher, R., Naef, U., Chen, D., Hoffmann, A. M. & Somaini, B.

(1990). Malaria chemoprophylaxis among European tourists in tropical Africa: use, adverse reactions, and efficacy. *Bulletin of the World Health Organization*, **68**, 313–322.

Stricker, M., Steffen, R., Hornung, R., Gutzwiller, F., Eichmann, A. & Witassek, F. (1990). Flüchtige sexuelle Kontakte von Schweizer Touristen in den Tropen. *Münchner Medizinische Wochenschrift*, **132**, 175–178.

Taylor, D. N., Pollard, R. A. & Blake, P. A. (1983). Typhoid in the United States and the risk to the international travelers. *Journal of Infectious Diseases*, **148**, 599–602.

USA (1989). *Health Information for International Travel*. Atlanta, Georgia: US Department of Health and Human Services, Centers for Disease Control.

WHO (1988). *Diarrhoeal Diseases Control Programme—Drugs in the Management of Acute Diarrhoea in Infants and Young Children*. Geneva: World Health Organization, mimeographed document WHO/CDD/CMT/86.1, revision 1.

WHO (1989). Prophylactic and therapeutic use of mefloquine. *Weekly Epidemiological Record*, **32**, 247–248.

WHO (1991). *International Travel and Health: Vaccination Requirements and Health Advice*. Geneva: World Health Organization, p. 75.

4. Cosmologies and pharmacologies

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